

Amendment C
Application No. 09/271,411

Attorney Docket No. 22660-0009P1

30. (amended) The device of claim 23, wherein the portion of the body forming the transition region is narrower than the portion of the body forming the reaction chamber.

c14
Please amend claim 31 as follows:

31. (amended) The device of claim 23, wherein the body defines air pockets surrounding the transition region.

c15
Please amend claim 36 as follows:

36. (amended) The device of claim 23, wherein the body further has formed therein at least one side channel communicating with the transition region, and wherein the device further includes at least one flow controller in the side channel for controlling the flow of fluids through the side channel.

REMARKS

This amendment is identical to that submitted July 31, 2001 except that the instruction to cancel claims 24 and 27 now appears under the section entitled "IN THE CLAIMS". In the amendment of July 31, the instruction was only given in the "REMARKS" section. Entry of the amendment and allowance of all pending claims is requested.

The title, specification, and claims have been amended to delete the word "unitary" which word was found to be confusing and contradictory by the Examiner.

Claim 27 has been rewritten in independent form (as newly amended claim 23) which the Examiner indicated would be allowable. Previous claims 24 and 27 have been canceled since the subject matter of these claims is incorporated into amended claim 23.

Claims 29 and 31 have been amended to overcome the 112 rejection given in the last office action.

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Please cancel claims 41-44 without prejudice to expedite the issuance of claims 23-40. Applicant will continue prosecution of the subject matter of claims 41-44 in a continuation application.

Claims 26, 32-35, and 37-40 are unchanged.

Thus, the present application complies with all of the Examiner's requirements for allowance, which action the applicant kindly requests.

ATTACHMENTS

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

Respectfully submitted,



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#312191 v1 - 22660-0009P1 Amendment after Final Rejection

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE TITLE:

Please replace the title with the following title:

--[UNITARY] CHEMICAL PROCESSING DEVICE--

IN THE SPECIFICATION:

Please replace the paragraph beginning at page 4, line 22, with the following paragraph:

--In a preferred embodiment, the device comprises a [unitary] body, preferably a molded polymeric part, having formed therein a reaction chamber for chemically reacting a sample, a separation region for separating components of the sample, and a transition region connecting the reaction chamber to the separation region. The reaction chamber, transition region, and separation region are formed in and enclosed by the [unitary] body. Additionally, the transition region includes at least one flow restrictor for controlling the flow of fluid between the reaction chamber and the separation region. Further, the portion of the [unitary] body defining the transition region has lower thermal conduction than the portion of the body defining the reaction chamber so that the transition region substantially thermally isolates the reaction chamber from the separation region.--

Please replace the paragraph beginning at page 5, line 4, with the following paragraph:

--The [unitary] body may be surrounded by external, functional components such as differential pressure sources, electro-motive sources, heaters, light sources, and optical detectors. In the preferred embodiment, the reaction chamber is an amplification chamber for amplifying nucleic acid in the sample. Also in the preferred embodiment, the separation region comprises an electrophoresis column or capillary containing a suitable matrix material, such as electrophoresis gel or buffer, for separating nucleic acid fragments in the sample.--

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Please replace the paragraph beginning at page 5, line 16, with the following paragraph:

--Fig. 1 is a schematic view of a [unitary] processing device having an integrated reaction chamber, transition region, and capillary electrophoresis separation region according to one embodiment of the present invention.--

Please replace the paragraph beginning at page 6, line 13, with the following paragraph:

--The present invention provides an integrated device for the processing of a fluid sample. The device comprises a reaction chamber, a product separation region, and a fluid transition region connecting the reaction chamber to the separation region. In the preferred embodiment, the reaction chamber, transition region, and separation region are formed in and enclosed by a [single unitary] body, preferably a molded piece of polymeric material. [The term "unitary" is herein intended to mean that the body of the device that forms the reaction chamber, transition region, and separation region is a single piece of material. This unitary design enables inexpensive, mass production of the device.]--

Please replace the paragraph beginning at page 7, line 22, with the following paragraph:

--Fig. 1 shows one embodiment of a processing device 2 formed by a [unitary] body 4. The body 4 has formed therein a reaction chamber 6, a separation region 8, and a transition region 10 connecting the reaction chamber to the separation region. The reaction chamber 6 has an inlet port 12 for adding sample and reagents as required by the particular reaction performed in the chamber. The device 2 may include an outlet port as well as the inlet port 12. The ports may serve to connect the device to an external pump, vacuum source, or syringe. Alternatively, the ports may function as vents. In this embodiment, the separation region 8 is a capillary electrophoresis tube 14 containing appropriate separation material, e.g. electrophoresis gels or polymers, for separating components of the sample. Such separation materials are well known in the art.--

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Please replace the paragraph beginning at page 8, line 4, with the following paragraph:

--The integrated device 2 also includes an injection electrode 20 and a separation electrode 22 embedded in the [unitary] body 4. The electrodes 20 and 22 are located at opposite ends of the device to drive electrophoretic, electro-osmotic, or IEF ion flow through the separation region 8. Each electrode is preferably embedded in the body 4 such that one end of the electrode protrudes through an external surface of the body and such that the other end of the electrode protrudes into an internal region of the body.--

Please replace the paragraph beginning at page 10, line 13, with the following paragraph:

--Flow between the reaction chamber and the separation region may be by differential pressure, hydrodynamic forces, electrical motive forces, capillary action, pneumatic forces, hydraulic forces, mechanical forces, etc. The [unitary] device may be coupled to instruments to actuate fluid flow such as pumps, vacuums, electrical connections, and the like. Electromotive mobility of molecules, and especially nucleic acids, as in isoelectric focus and electrophoretic mobility, is a convenient movement mechanism because of the predictability of movement. When conditions such as buffer ionic strength, channel dimensions, gel type and density, current density, voltage drop, time, etc. are constant, it is relatively easy to predict the location of molecules. Under controlled conditions, at time (T), the position of the analyte should be at position (X) consistently. This concept is illustrated in Fig. 5 in which site 114 denotes the location of the target.--

Please replace the paragraph beginning at page 11, line 25, with the following paragraph:

--The electrodes may be embedded into the [unitary] device with little additional cost by several techniques. First, metal electrodes can be situated inside a plastic injection molding production machine and "over-molded" during the injection molding process. Second, the metal electrodes may be selectively screen-printed, or otherwise deposited by plating, thin-film deposition, etc., and patterned on the [unitary] body of the device. For example, one end of a screen-printed metal line may be used to contact fluid in the device while the other end forms a connector which is electrically engaged by an external instrument. Both of these techniques, and other similar techniques are cost-effective and very suitable for high-volume production lines.

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The electrodes are preferably located near vents which allow the venting of gases generated during the application of the high electric fields associated with electrophoresis. The vent ports could be simple openings in the tube itself or gas permeable hydrophobic membranes such as Gore-Tex®.--

Please replace the paragraph beginning at page 13, line 21, with the following paragraph:

--Electrodes positioned in the transition region and areas prior to the transition region, e.g., the reaction chamber 40, may facilitate movement of fluid into the transition region 60. Embedded electrodes 70A, 70B are shown by the form of the two-way valve configuration in Figure 3C. The electrode 70A is embedded in the reaction region 40 and the second electrode 70B is embedded in a channel 72 immediately downstream from the valve 64. The electrodes 70A, 70B protrude through the [unitary] body of the device to be partially exposed to the fluid inside of the chamber and channel.--

Please replace the paragraph beginning at page 20, line 7, with the following paragraph:

--The devices of the present invention may be produced by injection molding, casting, machining or other convenient means of making a one-piece body without bonding multiple pieces together. Molding allows for formation of a contiguous reaction chamber, transition region, and separation region. Valve structures may also be included in the mold, or in the alternative, added to device after the [unitary] body is molded.--

Please replace the paragraph beginning at page 21, line 8, with the following paragraph:

--Furthermore, electrodes may be "overmolded" by partially inserting electrodes at their selected locations into the mold such that the electrodes become embedded in the [unitary] body after the material is added to the mold and allowed to solidify. The electrodes may be made of platinum, silver, carbon, gold or any other suitable electrically conductive material. Other components may be optionally overmolded to the device in a similar fashion.--

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Please replace the paragraph beginning at page 21, line 15, with the following paragraph:

--In the alternative, after the [unitary] body is formed, electrodes, filters, resistive heating elements, etc. may be embedded into the body using screen-printing or thin-film depositing techniques. Reagents, matrices or fluids may be injected into various reservoirs and channels of the formed body. Furthermore, the device may include components external to the [unitary] body, such as optics, electrical connections to the electrodes, heater(s) embedded in the body, pneumatic interfaces to pumps or vacuums, etc. Alternatively, such components may be located in an external instrument into which the [unitary] device is placed for sample processing, as described above.

Please replace the paragraph beginning at page 21, line 24, with the following paragraph:

--To summarize, the entire assembly of the reaction chamber, transition region, and separation region are preferably formed in a [single, unitary,] disposable body. There are a number of reasons why the device of the present invention is much improved over prior implementations.

- 1) the entire device is disposable, so that sample carry-over and contamination from sample to sample is not a problem;
- 2) all major elements of the device are integrated into one analytical component; it is not necessary to transfer the sample or the reaction products from one device having a reaction chamber to a separate device having a separation tube;
- 3) provision is made for thermally isolating the reaction chamber from the separation region, thereby ensuring proper heating of a sample and operability of the separation region;
- 4) provision is made for optical detection both in the reaction chamber as well as the separation tube;
- 5) provision is made for venting and otherwise dealing with the gases generated during electrophoresis or during isoelectric focusing;
- 6) the inconvenience of bonding techniques to connect substrates and modules is avoided; and
- 7) embedded electrodes provide for reproducibility and low cost mass production.--

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IN THE CLAIMS:

Applicant requests amendment of the claims to comply with the Examiner's conditions for allowance as follows:

Please amend claim 23 as follows:

23. (amended) A device for processing a sample, the device comprising a [unitary] body having formed therein:
- a) a reaction chamber for chemically reacting the sample;
 - b) a separation region for separating components of the sample; [and]
 - c) a transition region connecting the reaction chamber to the separation region[.]; wherein the reaction chamber, transition region, and separation region are formed in and enclosed by the [unitary] body, the device further includes at least one flow restrictor in the transition region for controlling the flow of fluid between the reaction chamber and the separation region, and the portion of the [unitary] body defining the transition region has [lower] sufficiently low thermal conduction [than the portion of the body defining the reaction chamber] so that the transition region substantially thermally isolates the reaction chamber from the separation region[.]; and
 - d) at least two electrodes coupled to the body, the electrodes being positioned to force the sample to flow from the reaction chamber or from the transition region into the separation region when a voltage difference is applied between the electrodes;
- wherein the device is in combination with and designed to be inserted into an instrument having a heater for heating the reaction chamber and having electrical connections for applying the voltage difference between the electrodes.

Please amend claim 25 as follows:

25. (amended) The device of claim [24] 23, wherein the [unitary] body comprises a molded polymeric part having the electrodes embedded therein.

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Please amend claim 28 as follows:

28. (amended) The combination of claim [27] 23, wherein the instrument further includes optics for detecting separated components of the sample or for optically monitoring the reaction chamber.

Please amend claim 29 as follows:

29. (amended) The device of claim 23, [further comprising] wherein the device comprises:
- a) a first electrode embedded in the body adjacent the reaction chamber;
 - b) a second electrode embedded in the body adjacent the transition region;
 - c) a third electrode embedded in the body adjacent the separation region; and
 - d) a high molecular weight filter positioned in the transition region such that when a voltage is applied between the first and second electrodes, components in the sample are transported from the reaction chamber to the transition region and collected on the filter, and such that when a subsequent voltage is applied between the second and third electrodes, the components collected on the filter are transported into the separation region.

Please amend claim 30 as follows:

30. (amended) The device of claim 23, wherein the portion of the [unitary] body forming the transition region is narrower than the portion of the body forming the reaction chamber.

Please amend claim 31 as follows:

31. (amended) The device of claim 23, wherein the body defines air pockets [adjacent] surrounding the transition region.

Please amend claim 36 as follows:

36. (amended) The device of claim 23, wherein the [unitary] body further has formed therein at least one side channel communicating with the transition region, and wherein the device further includes at least one flow controller in the side channel for controlling the flow of fluids through the side channel.